REMARKS

Amendments to the Claims

Claims 1, 3-5, 7, 8, 11, 12, 14 and 15 have been amended.

Claims 26-32 have been added.

Claims 16-20, 22 and 25 have been canceled.

Claims 1, 3, 4, 5, 7, 8, 11, 12, 14 and 15 have been amended to recite TNFα-mediated "viral infection," and to delete reference to hepatitis. Support for these claim amendments is found in the specification, for example at page 58, lines 5-9. In addition, support is found in priority application 07/670,827, filed March 18, 1991, at page 10, line 22 to page 11, line 4. This priority application is incorporated in the subject application by reference on page 1, lines 4-21.

Claims 1, 3, 4, 5, 12 and 14 have been amended to recite that the antibody or antigen-binding fragment competitively inhibits binding of A2 to human TNFα. Reference to cA2 has been deleted. Support is found in the specification, for example, at page 19, line 17 to page 20, line 2 and page 30, lines 5-12. In addition, support is found in the specification of priority application US Serial No. 07/670,827, filed March 18, 1991, for example, at page 12, line 24 to page 13, line 4; page 14, lines 3-9; and page 19, lines 3-10.

Claims 11 and 15 have been amended to recite "epitopic specificity identical to A2...." Reference to cA2 has been deleted. Support is found in the specification, for example, at page 34, line 25 to page 35, line 4; and Example X, particularly page 80, lines 14-23. In addition, support is found in the specification of priority application US Serial No. 07/670,827, filed March 18, 1991, for example, Example X at page 67, line 14 to page 68, line 2.

Claims 1, 3, 4, 5, 11, 12, 14 and 15 have been further amended to recite "ATCC Accession No. PTA-7045" Support for these amendments is found in the specification, as amended, for example, at page 25, lines 16-23. In addition, support for reference to the cell line for the A2 antibody is found in the priority application US Serial No. 07/670,827, filed March 18, 1991, at page 19, lines 14-20.

Claims 1, 3, 4, 5, 11, 12, 14 and 15 have been further amended to recite that the antibody or antigen-binding fragment "binds to a neutralizing epitope of human TNFα *in vivo* with an affinity of at least 1 x 10^8 liter/mole, measured as an association constant (Ka), as determined by Scatchard analysis." Support is found in the specification, for example, at page 21, lines 16-23; page 60, line 25 to page 61, line 5; and Example X, particularly at page 80, line 24 to page 81,

line 12. In addition, support is found in the specification of priority application US Serial No. 07/670,827, filed March 18, 1991, for example, at page 13, lines 5-8; page 18, lines 17-19; page 20, lines 3-6; and Example X, particularly, at page 67, line 12 to page 68, line 25.

Claims 1, 3, 5, 11, 12, 14 and 15 have been amended to recite "antigen-binding fragment." Support is found in the specification, for example, at page 9, lines 8-11 and page 17, lines 2-8. In addition, support is found in the specification of priority application US Serial No. 07/670,827, filed March 18, 1991, for example, at page 1, lines 5-12 and page 11, lines 10-20.

Claims 1, 3, 12, 14 and 15 have been further amended to recite "human constant region." Claims 4 and 5 have been amended to recite "human IgG1" constant region. Support is found in the specification, for example, at page 10, lines 8-15; page 31, line 6 to page 32, line 2; and page 34, lines 16-21. In addition, support is found in the specification of priority application US Serial No. 07/670,827, filed March 18, 1991, for example, at page 9, lines 21-23; page 12, lines 18-26; page 26, lines 6-19; and page 52, lines 18-20.

New Claim 26 is directed to the method of Claim 1, wherein said TNFα-mediated viral infection is associated with liver inflammation. New Claim 27 is directed to the method of Claim 1, wherein said TNFα-mediated viral infection is associated with inflammation. New Claim 28 is directed to the method of Claim 1, wherein said TNFα-mediated viral infection is associated with alcohol-induced hepatitis. Support for these new claims is found in the specification, for example, page 57, lines 22-25; page 58, lines 5-9 and page 59, line 11. In addition, support is found in priority application 07/670,827, filed March 18, 1991, at page 10, line 22 to page 11, line 4; page 26, lines 6-8; and page 39, line 20 to page 40, line 9.

New Claim 29 is directed to the antibody or antigen-binding fragment of Claim 1, which is of immunoglobulin class IgG1, IgG2, IgG3, IgG4 or IgM. Support is found in the specification, for example, at page 17, lines 19-21; page 31, lines 6-13; and page 125, lines 14-17. In addition, support is found in the specification of priority application US Serial No. 07/670,827, filed March 18, 1991, for example, at page 26, lines 6-19.

New Claim 30 recites "The antigen-binding fragment of Claim 1, wherein said fragment is selected from the group consisting of Fab, Fab', $F(ab')_2$ and Fv." Support is found in the specification, for example, at page 26, line 4. In addition, support is found in the specification of

priority application US Serial No. 07/670,827, filed March 18, 1991, for example, at page 20, lines 16-19.

New Claim 31 is directed to the antibody or antigen-binding fragment of Claim 1, wherein the antibody or antigen-binding fragment comprises a human constant region and a human variable region. Support is found in the specification, for example, at page 9, lines 8-11; and page 31, line 3 to page 32, line 2. In addition, support is found in the specification of priority application US Serial No. 07/670,827, filed March 18, 1991, for example, at page 12, lines 8-25.

New Claim 32 is directed to the antibody or antigen-binding fragment of Claim 1, which comprises at least one human light chain and at least one human heavy chain. Support is found in the specification, for example, at page 19, lines 1-6; and page 31, line 3 to page 32, line 2. In addition, support is found in the specification of priority application US Serial No. 07/670,827, filed March 18, 1991, for example, at page 12, lines 8-25.

No new matter has been added by the amendments. Therefore, entry of the amendments into the application is respectfully requested.

Amendments to the Specification

The title and abstract have been amended to recite "viral infection" to be more descriptive of the claims, as amended. Support for this amendment can be found in the specification, for example, at page 10, lines 16-25; page 16, lines 9-15; and page 57, line 17 to page 59, line 14. In addition, support is found in priority application 07/670,827, filed March 18, 1991, at page 10, line 22 through page 11, line 9 and page 26, lines 6-10. This priority application is incorporated in the subject application by reference on page 1, lines 4-21.

In addition, as discussed below, the paragraph at page 58, line 1 through page 59, line 14 has been amended to delete reference to "hepatitis", and to refer solely to "alcohol-induced hepatitis." Support for this Amendment is found in the specification, for example, at page 58, line 1 through page 59, line 14 as originally-filed. In addition, support is found in priority application 07/670,827, filed March 18, 1991, at page 10, line 22 to page 11, line 4.

Further, Applicants have amended the specification to correct the spelling of "Geysen" on page 86, line 26 to page 87, line 12. Applicants submit evidence that the correct spelling is "Geysen" in the enclosed Abstract (Exhibit A).

Lastly, Applicants have amended the specification to recite "ATCC Accession No. PTA-7045," and to recite that c134A was deposited pursuant to the Budapest Treaty requirements with the American Type Culture Collection (ATCC), 10801 University Boulevard, Manassas, Virginia 20110-2209, on September 22, 2005. Support for these amendments is found in the specification, as amended, for example, at page 25, lines 16-23. In addition, support for reference to the cell line for the A2 antibody is found in the priority application US Serial No. 07/670,827, filed March 18, 1991, at page 19, lines 14-20.

No new matter has been added by the amendments. Therefore, entry of the amendments into the application is respectfully requested.

Priority

The Examiner states that "[t]he filing date of the instant claims is deemed to be the filing date of the instant application...." According to the Examiner, "[n]either the priority applications nor the instant application [ ] provides a sufficient description of a representative number of species to represent the entire genus of 'hepatitis' or 'TNF-α-mediated hepatitis', as currently claimed" (emphasis omitted).

While Applicants respectfully disagree with the Examiner's position and reserve their rights to file continuing or divisional applications to pursue these claims, in order to further prosecution, as discussed above, Claim 17, which recited "hepatitis", has been canceled. Claims 1, 3-5, 7, 8, 11, 12, 14 and 15 have been amended to recite "TNFα-mediated viral infection." As discussed above, support for these claim amendments is found in the specification of priority application 07/670,827, filed March 18, 1991, at page 10, line 22 to page 11, line 4.

Therefore, the priority application 07/670,827 (filed March 18, 1991) provides sufficient written description and enablement for Applicants' claimed methods of treating viral infection, and Applicants are entitled to claim the benefit of it. This priority application has been properly referenced on page 1 of the specification in compliance with 35 U.S.C. § 120.

Objection Under 35 U.S.C. § 132

The Amendment filed April 6, 2005 is objected to under 35 U.S.C. § 132 on the grounds that it introduces new matter into the disclosure. The Examiner states that "[t]he added material which is not supported by the original disclosure is as follows: 'hepatitis' or 'TNF-α-mediated

hepatitis.'" Further, the Examiner states that "Applicant is required to cancel the new matter in the reply to this Office Action." While Applicants respectfully disagree with the Examiner's position and reserve their rights to file continuing or divisional applications to pursue these claims, in order to further prosecution, the paragraph at page 58, line 1 through page 59, line 14 has been amended to delete reference to "hepatitis." In addition, Claims 16-19, 20, 22 and 25 have been canceled and Claims 1, 3-5, 7, 8, 11, 12, 14 and 15 have been amended to recite TNFα-mediated "viral infection." Thus, the objection is moot.

Reconsideration and withdrawal of the objection are respectfully requested.

Rejection of Claims 1, 3-5, 7-12 and 14-25 Under 35 U.S.C. § 112, first paragraph

Claims 1, 3-5, 7-12 and 14-25 have been rejected under 35 U.S.C. § 112, first paragraph as lacking written description. The Examiner states that "[t]he specification as originally filed does not provide support for the invention as now claimed: 'hepatitis' or 'TNF-α-mediated hepatitis.'"

While Applicants respectfully disagree with the Examiner's position and reserve their rights to file continuing or divisional applications to pursue these claims, in order to further prosecution, Claims 16-20, 22 and 25 have been canceled. Claims 1, 3-5, 7, 8, 11, 12, 14 and 15 have been amended to recite TNFα-mediated "viral infection", thereby rendering the rejection moot. Support for these claim amendments is found in the specification, for example at page 58, lines 5-9. In addition, support is found in priority application 07/670,827, filed March 18, 1991, at page 10, line 22 to page 11, line 4.

Therefore, both the current application and the priority application 07/670,827 (filed March 18, 1991) provide sufficient written description for Applicants' claimed methods of treating viral infection, and Applicants are entitled to claim the benefit of it.

Reconsideration and withdrawal of the rejection are respectfully requested.

Rejection of Claims 1, 3-5, 7-12 and 14-25 Under 35 U.S.C. § 112, first paragraph

Claims 1, 3-5, 7-12 and 14-25 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The Examiner states that the cA2 antibody must be known and readily

available to the public, or obtainable by a repeatable method set for in the specification, or else a deposit of the cell line/hybridoma may be made in order to satisfy the enablement requirement.

37 C.F.R. § 1.809 (b)(1) states that "[t]he applicant for patent or patent owner shall reply to the rejection under paragraph (a) of this section by (1) In the case of an applicant for patent, either making an acceptable original...deposit, or assuring the Office in writing that an acceptable deposit will be made...." In addition, 37 C.F.R. § 1.809 (d) states that "[f]or each deposit made pursuant to these regulations, the specification shall contain: (1) The accession number for the deposit; (2) The date of deposit; (3) A description of the deposited biological material sufficient to specifically identify it and to permit examination; and (4) The name and address of the depository."

In order to expedite prosecution, and in accordance with 37 C.F.R. § 1.809 (b)(1), on September 22, 2005, Applicants deposited the cell line for the A2 antibody (designation c134A) with American Type Culture collection (ATCC) under the Budapest Treaty. The ATCC accession number is PTA-7045.

The specification at page 25, lines 16-23 has been amended to recite "As examples of antibodies according to the present invention, murine mAb A2 (ATCC Accession No. PTA-7045) of the present invention is produced by a cell line designated c134A." The specification at page 25, lines 16-23 has been further amended to recite "c134A was deposited pursuant to the Budapest Treaty requirements with the American Type Culture Collection (ATCC), 10801 University Boulevard, Manassas, Virginia 20110-2209, on September 22, 2005."

Further, Claims 16-20, 22 and 25 have been canceled. Claims 1, 3, 4, 5, 11, 12, 14 and 15 have been amended to delete reference to "cA2" and have been amended recite the ATCC accession number for the cell line of the A2 antibody. Dependent Claims 21, 23-24 and 26-32 depend from these claims and, therefore, contain the same limitation. Applicants reserve their rights to file continuing or divisional applications to pursue these claims.

Support for the amendments and the deposit of the cell line for the A2 antibody is found in the specification, for example, at page 25, lines 16-23. In addition, support is found in the priority application US Serial No. 07/670,827, filed March 18, 1991, at page 19, lines 14-20.

Filed concurrently herewith is Applicants' Attorney Statement Under 37 C.F.R. § 1.804, § 1.806 and § 1.808.

Reconsideration and withdrawal of the rejection are respectfully requested.

Rejection to Claims 1, 3-5, 7-12 and 14-25 Under 35 U.S.C. § 112, second paragraph

A) The Examiner has rejected Claims 1, 3-5, 7-12 and 14-25 as indefinite in the recitation of "cA2".

Specifically, the Examiner states that "the use of 'cA2' antibody as the sole means of identifying the claimed antibody renders the claim indefinite because 'cA2' is merely a laboratory designation which does not clearly define the claimed product, since different laboratories may use the same laboratory designation [ ] to define completely distinct hybridomas / cell lines."

While Applicants disagree with the Examiner's position and reserve their rights to file continuing or divisional applications to pursue these claims, in order to further prosecution, as discussed above, Claims 16-20, 22 and 25 have been canceled. Claims 1, 3, 4, 5, 11, 12, 14 and 15 have been amended to delete reference to cA2 and have been amended recite "ATCC Accession No. PTA-7045" for the cell line of the A2 antibody. As discussed above, on September 22, 2005, Applicants deposited the cell line for the A2 antibody with ATCC under the Budapest Treaty. The specification at page 25, lines 16-23 have been amended to recite the ATCC accession number, the date of deposit, a description of the biological material and the name and address of the depository. The Examiner has indicated that amending the claims to recite the appropriate ATCC Accession number would obviate this rejection.

Reconsideration and withdrawal of the rejection are respectfully requested.

B) Applicants acknowledge obviation of the prior rejection with respect to hepatitis pathologies.

C) Claims 1, 3-5, 7-12 and 14-25 have been rejected as indefinite under 35 U.S.C. § 112, second paragraph.

The Examiner states that "the metes and bounds of said 'TNFα-mediated hepatitis' is ill-defined and ambiguous."

While Applicants disagree with the Examiner's position and reserve their rights to file continuing or divisional applications to pursue these claims, in order to further prosecution, as discussed above, as discussed above, the paragraph at page 58, line 1 through page 59, line 14

has been amended to delete reference to "hepatitis." In addition, Claims 16-20, 22 and 25 have been canceled. Claims 1, 3-5, 7, 8, 11, 12, 14 and 15, as amended, no longer recite "TNFα-mediated hepatitis," thereby rendering the rejection moot.

Reconsideration and withdrawal of the rejection are respectfully requested.

D) The Examiner states that "Claims 16 and 18-19 are indefinite in the recitation of 'neutralizing epitope of human TNFα'...."

While Applicants disagree with the Examiner's position and reserve their rights to file continuing or divisional applications to pursue these claims, in order to further prosecution, as discussed above, Claims 16 and 18-19 have been canceled, thereby rendering the rejection moot. Reconsideration and withdrawal of the rejection are respectfully requested.

Rejection of Claims 1, 3-5, 7-12 and 14-25 Under 35 U.S.C. § 102(b)

The Examiner has rejected Claims 1, 3-5, 7-12 and 14-25 under 35 U.S.C. § 102(b) as being anticipated by Le *et al.* (U.S. Patent No. 5,919,452). The Examiner states that:

> Le *et al.* teach methods of treating TNF-α-mediated diseases, including alcohol-induced hepatitis (see column 35, line 12) with TNF-α-specific antibodies, including recombinant and chimeric antibodies and the cA2 antibody specificity of the instant invention... Applicant is reminded that no more of the reference is required than that it sets forth the substance of the invention. The claimed functional limitations would be inherent properties of the referenced methods to treat alcohol-induced hepatitis with recombinant cA2-specific antibodies. A species anticipates a claim to a genus.

See MPEP 2131.02.

While Applicants respectfully disagree with the Examiner's position and reserve their rights to file continuing or divisional applications to pursue these claims, in order to further prosecution, as discussed above, Claims 16-20, 22 and 25 have been canceled. Claims 1, 3-5, 7, 8, 11, 12, 14 and 15 have been amended to recite TNFα-mediated "viral infection", thereby rendering the rejection moot. As discussed above, support for these claim amendments is found in the specification, for example at page 58, lines 5-9. In addition, support is found in priority application 07/670,827, filed March 18, 1991, at page 10, line 22 to page 11, line 4.

Further, Applicants note that the Examiner has cited as prior art one of Applicants' priority patents (U.S. Patent No. 5,919,452). Le *et al.* (U.S. Patent No. 5,919,452) is not prior art

under 35 U.S.C. § 102 (b) because it was not published more than one year before Applicants' priority date. As discussed above, Applicants are entitled to a priority date before the 35 U.S.C. § 102(b) date of U.S. Patent No. 5,919,452. Specifically, as discussed above, Applicants are entitled to priority to U.S. Application Serial No. 07/670,827 (filed March 18, 1991). Furthermore, the subject application is substantially identical to U.S. Patent No. 5,919,452, lists the same inventors and claims the benefit of priority to the same U.S. priority application (U.S. Serial No. 07/670,827) as U.S. Patent No. 5,919,452. Hence, Le *et al.* U.S. Patent No. 5,919,452 is not prior art.

Reconsideration and withdrawal of the rejection are respectfully requested.

CONCLUSION

In view of the above amendments and remarks, it is believed that all claims are in condition for allowance, and it is respectfully requested that the application be passed to issue. If the Examiner feels that a telephone conference would expedite prosecution of this case, the Examiner is invited to call the undersigned.

Respectfully submitted,

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